

We claim:

1. A targeting construct comprising:
 - (a) a first polynucleotide sequence homologous to a limulus clotting factor protease-like gene;
 - (b) a second polynucleotide sequence homologous to the limulus clotting factor protease-like gene; and
 - (c) a selectable marker.
2. The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
3. A method of producing a targeting construct, the method comprising:
 - (a) providing a first polynucleotide sequence homologous to a limulus clotting factor protease-like gene;
 - (b) providing a second polynucleotide sequence homologous to the limulus clotting factor protease-like;
 - (c) providing a selectable marker; and
 - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
4. A method of producing a targeting construct, the method comprising:
 - (a) providing a polynucleotide comprising a first sequence homologous to a first region of a limulus clotting factor protease-like gene and a second sequence homologous to a second region of a limulus clotting factor protease-like gene;
 - (b) inserting a positive selection marker in between the first and second sequences to form the targeting construct.
5. A cell comprising a disruption in a limulus clotting factor protease-like gene.
6. The cell of claim 5, wherein the cell is a murine cell.
7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.
8. A non-human transgenic animal comprising a disruption in a limulus clotting factor protease-like gene.
9. A cell derived from the non-human transgenic animal of claim 8.
10. A method of producing a transgenic mouse comprising a disruption in a limulus clotting factor protease-like gene, the method comprising:
 - (a) introducing the targeting construct of claim 1 into a cell;
 - (b) introducing the cell into a blastocyst;

- (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
- (d) breeding the chimeric mouse to produce the transgenic mouse.

11. A method of identifying an agent that modulates the expression of a limulus clotting factor protease-like, the method comprising:

- (a) providing a non-human transgenic animal comprising a disruption in a limulus clotting factor protease-like gene;
- (b) administering an agent to the non-human transgenic animal; and
- (c) determining whether the expression of limulus clotting factor protease-like in the non-human transgenic animal is modulated.

12. A method of identifying an agent that modulates the function of a limulus clotting factor protease-like, the method comprising:

- (a) providing a non-human transgenic animal comprising a disruption in a limulus clotting factor protease-like gene;
- (b) administering an agent to the non-human transgenic animal; and
- (c) determining whether the function of the disrupted limulus clotting factor protease-like gene in the non-human transgenic animal is modulated.

13. A method of identifying an agent that modulates the expression of limulus clotting factor protease-like, the method comprising:

- (a) providing a cell comprising a disruption in a limulus clotting factor protease-like gene;
- (b) contacting the cell with an agent; and
- (c) determining whether expression of the limulus clotting factor protease-like is modulated.

14. A method of identifying an agent that modulates the function of a limulus clotting factor protease-like gene, the method comprising:

- (a) providing a cell comprising a disruption in a limulus clotting factor protease-like gene;
- (b) contacting the cell with an agent; and
- (c) determining whether the function of the limulus clotting factor protease-like gene is modulated.

15. The method of claim 13 or claim 14, wherein the cell is derived from the non-human transgenic animal of claim 8.

16. An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.

17. A transgenic mouse comprising a disruption in a limulus clotting factor protease-like gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: increased pain threshold or increased susceptibility to seizures as compared to wild-type mice.
20. A method of producing a transgenic mouse comprising a disruption in a limulus clotting factor protease-like gene, wherein the transgenic mouse exhibits at least one of the following increased pain threshold or increased susceptibility to seizures, the method comprising:
 - (a) introducing a limulus clotting factor protease-like gene targeting construct into a cell;
 - (b) introducing the cell into a blastocyst;
 - (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
 - (d) breeding the chimeric mouse to produce the transgenic mouse comprising a disruption in a limulus clotting factor protease-like gene.
22. A cell derived from the transgenic mouse of claim 17.
23. A method of identifying an agent that ameliorates a phenotype associated with a disruption in a limulus clotting factor protease-like gene, the method comprising:
 - (a) administering an agent to a transgenic mouse comprising a disruption in a limulus clotting factor protease-like gene; and
 - (b) determining whether the agent ameliorates at least one of the following phenotypes: : increased pain threshold or increased susceptibility to seizures as compared to wild-type mice.
24. A method of identifying an agent which modulates limulus clotting factor protease-like expression, the method comprising:
 - (a) administering an agent to the transgenic mouse comprising a disruption in a limulus clotting factor protease-like gene; and
 - (b) determining whether the agent modulates limulus clotting factor protease-like expression in the transgenic mouse, wherein the agent has an effect on at least one of the following increased pain threshold or increased susceptibility to seizures as compared to wild-type mice.
25. A method of identifying an agent which modulates limulus clotting factor protease-like gene function, the method comprising:
 - (a) providing a cell comprising a disruption in a limulus clotting factor protease-like gene;

- (b) contacting the cell with an agent; and
- (c) determining whether the agent modulates limulus clotting factor protease-like gene function, wherein the agent modulates a phenotype associated with a disruption in a limulus clotting factor protease-like gene.

26. The method of claim 35, wherein the phenotype comprises at least one of the following: increased pain threshold or increased susceptibility to seizures as compared to wild-type mice.

27. An agent identified by the method of claim 23, claim 24, or claim 25.

28. An agent that modulates the function, expression or activity of a limulus clotting factor protease-like gene.

29. A method of ameliorating a condition associated with increased susceptibility to seizures, the method comprising administering to a subject in need, a therapeutically effective amount of an agent that modulates limulus clotting factor protease-like function, expression or activity.

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